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CHRONIC INFLUENZA AND ITS RELATION TO NEUROPATHY.

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My thesis is that influenza may be and frequently is a chronic intoxication.

The specificity of influenza was discovered in 1902, by Pfeiffer, more than four hundred years after epidemics of the disease were first accurately described. Most authorities state that the rate of mortality is very low, and the disease has presented little of general interest aside from its pandemicity, vagaries of onset and manifestations, and its multiplicity of complications. The mode of invasion is conceded to be through the respiratory tract, and the organism is usually found in the bronchial and nasal secretions. The bacilus often persists in secretions after subsidence of symptoms in severe cases. I have been much impressed with the belief that influenza might be a chronic, as well as acute infection, or, at least, a chronic intoxication, and my beliefs, while not proved by extensive clinical experience and data, have, at least, been partially corroborated by the general history of many cases of "grippe," reported by reliable investigators. In explanation of the frequent occurrence of Bacillus influenzæ in the secretions of persons in normal health, or suffering from some other disease, such as tuberculosis, scarlet fever, measles, etc., attention may be called to the analogous occurrence of the causative organism of enteric fever, diphtheria, and cholera in persons not suffering from these diseases.

In order to throw more light on the cause and dissemination of epidemic influenza, B. Scheller made examinations of a large number of persons suffering from epidemic influenza, as well as apparently normal persons in Königsberg during the winters of 1906-07, 1907-08, 1908-09, and the summer of 1908. Swabs from the throats of cases diagnosticated clinically as influenza, cases of pulmonary tuberculosis, and normal individuals were examined, microscopically and culturally, for Bacillus influenzæ. During an epidemic of influenza in the winter of 1906-07, 80 per cent. of the 56 cases of influenza showed the presence of Bacillus influenzæ in pure culture in more than one-half the cases; 8 cases wrongly diagnosticated as tuberculosis, and 4 of pneumonia showed pure cultures of Bacillus influenzæ. Of 109 normal persons examined, 25 (24 per cent.) were found to be "carriers" of Bacillus influenzæ, 15 of these giving a history of at least one previous attack of the disease.

Osler, in his monograph on influenza, concludes that "since the late severe epidemics it has been the fashion to date various ailments or chronic ill-health from the disease." In many cases the deduction is certainly correct. It is astonishing to note the number of patients who have been crippled in health for years after an attack.

Chronic influenza in many respects certainly bears a close similarity to tuberculosis, and I have no doubt that many cases of chronic capillary bronchitis, pneumonia, bronchiectasis, etc., in which the disturbing factor was Bacillus influenzæ, have been diagnosticated tuberculosis. This has, in a way, been confirmed by my study of three cases, which clinically presented symptoms and physical signs of tuberculosis, but in which the tubercle bacillus could not be isolated.

At autopsy the following results were found:

CASE I.—Pericarditis with serous effusion; bronchiectasis.

CASE II.—Carnification of the tip of the right lower lobe of the lung; hepatic enlargement, non-caseating nodules; complete fibrosis of the ovaries; and intramural fibrosis of the uterus.

CASE III.—Capillary bronchitis; atheroma of the aorta; sclerotic endocarditis; fibrosis of the ovaries, and catarrhal enterocolitis.

I admit that the pathological findings in these cases are as insufficient and indefinite as the clinical diagnosis of tuberculosis was justifiable, although the organism was not found. The pathological results were such as we should expect in the cases which have been selected from clinical reports in the vast amount of literature. Attention is especially directed to the last two cases which presented a diffuse fibroid degeneration of the ovaries. This was certainly non-tuberculous. *Could it result from chronic influenza?* Authorities have always emphasized the distressing effects of "la grippe" on the female genitalia. No disease is more to be dreaded as an intercurrent affection during pregnancy or the puerperium, because of the frequency of abortion and the occurrence of menstrual irregularities.

F. T. Lord, the pioneer in the study of influenza as a chronic disease, has written an extensive paper on the pathological and clinical similarity and confusion of influenza with tuberculosis, during epidemic and interepidemic periods. Jacobson, by injecting influenza bacilli with streptococci, and Slatineano, by injecting them with lactic acid into laboratory animals, claim to have obtained virulent cultures, capable of killing animals. "It is possible in patients with Bacillus influenzæ in the sputa to get clumping of the bacilli suspended in normal saline solution (one-tenth or one-twentieth) of their blood serum." The results are inconstant.

Cantani also claims positive results, but his work has not been confirmed. The pathogenicity of Bacillus influenzæ has been substantiated by exhaustive bacteriological and biochemical studies. Although the results of animal inoculation are unsatisfactory, "the impression is irresistible that the influenza bacillus is pathogenic for man when, in sputum preparations or stained sections from the lungs of patients who have died of bronchopneumonia the bacilli are found in enormous numbers, both within and without the cells, to the practical exclusion of other organisms." Within the last few years the organism has been found as the apparent sole infecting agent in several extrapulmonary regions. Heroosky obtained pure cultures of Bacillus influenzæ from the pus of acute suppurative cholecystitis. Albrecht and Ghon found influenza bacilli as the only organism from a phlegmonous inflammation of the arm. Meunier, Nauwerk, and many others, report that the bacillus appeared to be the sole apparent cause of meningitis.

In man, therefore, the influenza bacillus must be regarded as capable of producing pathogenic processes without the aid of other organisms. The influenza bacillus must be regarded as the most important cause of a large number of cases of respiratory infection (acute and chronic) during the interepidemic periods; and as a contributing cause in many other cases when found mixed with the pneumococcus, Micrococcus catarrhalis, and other organisms

Patients may carry the organism in enormous numbers for years in their sputum, just as they have been shown to carry other common representatives of the flora of the respiratory tract. The frontal, ethmoid, and maxillary sinuses are frequently infected and act as the nidus of infection in chronic cases. Many physicians have observed cases of intermittent fever occurring periodically in which the diagnosis has been well-nigh impossible, even when assisted by chemical and bacteriological tests. Could these cases be acute exacerbations of a chronic infection or intoxication by Bacillus influenzæ?

Cerebrospinal meningitis while usually acute, may be intermittent or chronic, and Diplococcus intracellularis meningitidis can be isolated in pure culture by spinal puncture. Bacillus influenzæ has always shown a predilection for the nervous system. Numerous cases of meningitis have been reported, but it was not until a few years ago that the organism was isolated from the spinal fluid in influenzal meningitis. Certainly, if the organism can produce and be isolated from the exudate of spinal meningeal inflammation, we must presume a diffused hemotogenous dissemination. The diplococcus of Weichselbaum, producing acute or chronic meningitis, protects from recurrence. Influenzal infections do not protect, but rather predispose to recurrences. This, together with the clinical history of prolonged indisposition, with exacerbations at irregular intervals, is axiomatic evidence of chronicity.

Case I.—Mrs. P., female, white, aged sixty-two years, born in Virginia, has lived in Washington for the last fifty years. She gives history of no illness influencing the object of this report. She has had frequent colds in winter of each year for the last fifteen, before which time she was unusually hardy. In 1894 and 1895 she suffered from intermittent earache for several months; attacks being accompanied by headache and fever. The ear finally began discharging pus, and after a few weeks' treatment the discharge ceased, but the patient has since been quite deaf in the affected ear.

She came to me in December, 1907, suffering from what I presumed to be influenza, presenting the following symptoms: severe headache, lumbar pains, chills, fever, and cough, with mucopurulent expectoration. I gave the usual treatment for "grippe," to which she responded promptly. On the second day after leaving her bed she washed clothes all day, and on the following day I was again called.

The patient presented the same symptoms as before, but the cough was much more distressing and the expectoration profuse, fetid, and greenish yellow. The sputum examined for Bacillus tuberculosis was found negative. Urinalysis showed a slight trace of albumin.

Physical examination of chest showed numerous small, moist rales all over the chest, especially at the base, and bronchial fremitus. The breath sounds were harsh and arrhythmic at the base. The leukocyte count was 8300.

After remaining in bed several days under treatment, she was somewhat improved, but complained of great weakness, mental hebetude, indefinite neuralgic pains, and she looked apathetic. For two weeks she improved slowly, when, being exposed to damp, cold weather, she had a return of the cough and other symptoms. At this time, she showed the effects of these repeated attacks. She was anemic, had lost fifteen pounds in four weeks, was weak, and greatly depressed mentally. She continually expressed a willingness and desire to die, and her mental condition became distressing to her relatives. Another examination of the sputum for Bacillus tuberculosis was made. At this time I felt firmly convinced that my patient was suffering from pulmonary tuberculosis, but tubercle bacilli could not be demonstrated in the sputum after exhaustive examinations. I then examined smears of the nasal and bronchial secretions for Bacillus influenzæ and discovered an organism conforming in morphological and staining reactions to this organism. I then made glycerin-agar and ox-blood agar smear plates from the bronchial and nasal secretions, and found in mixed culture Bacillus influenzæ. The cough has persisted with more or less severity for the last year and a half, and patient has had at least ten attacks of influenza. Examinations of the sputum made on three occasions in the last four months, show a continuation of the bacillus.

CASE II.—S. F., a female, white, aged sixty-four years, has had two attacks, the second of the gastro-intestinal type. The organism was present in the nasal and bronchial discharges for three months after the last attack. She steadily lost weight, and since her last illness has had at irregular intervals attacks of pain in the right upper quadrant of the abdomen, resembling gallstone colic. There is no history of hepatic or gall-bladder infection prior to the "grippe" infection.

CASE III.—J. McB., male, white, aged fifty-eight years. In February, 1908, the patient was attended by me during a typical attack of influenza. No examination for the bacillus was made, but a localized epidemic prevailed in Washington at the time. The patient apparently made a prompt recovery from the acute symptoms, although tardy in regaining his strength and normal tone. In June of 1908, while attending the wife of the patient, he complained to me of loss in weight, apathy, and nervous instability; he said he "had chills at irregular intervals, followed by fever and drenching sweats." He suffered from dyspnœa on exertion, and had noticed for the past three months that his ankles became swollen toward evening. He appeared to have lost considerable weight, was anemic, and, in comparison to his robust appearance before his attack in February, was physically a derelict. Examination for Plasmodium malariæ was negative. Physical examination revealed marked increase in the area of cardiac dulness, with signs of mitral insufficiency and aortic stenosis.

He was put to bed and I called Dr. Thos. A. Claytor in consultation, who concurred in the findings as to heart, and in addition discovered the spleen markedly hypertrophied. The patient improved sufficiently to travel to Massachusetts, where he died several weeks after admission to a sanitarium.

The following cases excerpted from the literature are presented as bearing on influenza as a chronic infection.

F. C. Doble[1] reports a case of pericarditis and endocarditis appearing three days after very mild symptoms of influenza. The patient had a similar attack one year previous, and the physician (not Dr. Doble) told the patient he had "influenza of the heart." Doble says: "It is curious that the pericardium should be affected by so mild an attack of influenza, especially with slight bronchial symptoms. It seems to prove that Bacillus influenzæ circulates in the blood early in the disease in even a mild form and produces a true septicemia."

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[1] Lancet, April, 1908.

R. D. Brown[2] discusses at length the relative increase in psychoses during influenza. He says: "That cases of mental disease are increased by influenza cannot be disputed. It is well recognized that very frequently a certain amount of lassitude, neurasthenia, or mental depression is present long after an attack of influenza, though of mild character and short duration." A patient once with influenza during the fall or winter means a patient until spring or summer. It has been suggested that it is the postinfluenzal exhaustion that is the important factor, but although this may be true in some cases, it is not in all. The mental symptoms appear very often as soon as the second or third day of the disease. The influenza bacillus or its toxin seems to be the exciting agent rather than the fever of postfebrile exhaustion. A peculiar feature is the liability of postinfluenzal psychoses to relapse.

Clouston, in 1890, said: "The microbe or the poison of influenza destroyed the cortical energy to a much larger extent than any of the continued fevers or zymotics; nay, its effects on the mental condition of Europe, during the years of its prevalence, far exceeded in destructive powers all those diseases put together. . . . It left the mental and nervous tone of Europe lower by some degrees than it found it."

Bezly Thorne, in 1890, looked upon influenza as a cerebrospinal malady, and at that time this view was generally accepted. In nearly every case he had found some portion of the spine tender three or four hours after the onset of the attack. Gilbert Smith, at the same time, believed the morbific agent, howsoever originally produced, might be further developed in the human body and become the source of increased contagion. C. E. Abbot reports a case of "double attack," the first occurring January 18, 1890, and followed by rapid convalescence, the second on April 3, 1890.

Sansom has been one of the best investigators of influenza. He reports a case in a man, aged fifty-three years, with "recurrent attacks of hepatalgia without jaundice and protracted enfeeblement for twenty months after the acute attack contracted in Paris. He classifies his cases of prolonged pain as follows:

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[2] Scottish Med. Jour., 1902.

	Cases.
I. Epigastrium	9
Abdomen generally	2
Hepatic area localized	1
II. Head—various sites	7
Supra-orbital	1
Right inferior maxilla	1
III. Cardiac region	7
IV. Extremities—hips and legs	2
Calves	2
Arms	2
Right sciatic region	1
Fingers	1
Lumbar region	1

In all of these cases the symptoms of pain and protracted enfeeblement were almost constant from six months to as many years after the acute attack, and some patients had recurrence of general symptoms of influenza at intervals.

F. T. Lord[3] reports 11 chronic cases of influenza; "1 recovered, 1 died of cerebral hemorrhage, and 1 of chronic bronchiectasis and emphysema; 8 continued to cough with persistence of influenza bacilli in the sputa. "It is of interest to note that 5 of these patients were treated in the fall of 1902 at institutions for the cure of tuberculosis" (Lord).

The following cases, reported by F. T. Lord, are of great interest. Of 11 chronic cases, 2 died; 1 showed Bacillus influenzæ for a period of four years, during which time she had chronic cough. The autopsy revealed diffuse bronchiectasis and emphysema. A second patient had an asthmatic cough for nineteen months before admission and the organism persisted in the sputum for one month. He died two years after the attack. No autopsy was made. "Of the 9 cases followed one to three years, 8 showed no material improvement since they first came under observation." Their cough improves somewhat each summer, to return with equal intensity in the winter.

Between August, 1902, and January, 1904, Lord examined the sputum from cases coming to the out-patient department of the Massachusetts General Hospital. Cases were unselected, except to exclude from investigation those patients in whom Bacillus tuberculosis was found. Clinically they suffered from acute or chronic disease of the respiratory tract. In 110 (59 per cent.) of the 186 cases an organism having the morphology and staining reaction of Bacillus influenzæ was seen in varying numbers. In 56 cases (30 per cent. of all investigated) the organism was shown by culture to conform in all respects to the bacillus described by Pfeiffer in 1892, and regarded by him as the cause of epidemic influenza. In 47 cases (25 per cent. of all studied) the influenza bacilli were in overwhelming numbers. As the technique improved the organism was found in somewhat larger proportions. The cases showing the bacilli in the sputum were quite evenly distributed over the eighteen months during which the investigations were pursued. No epidemic of acute influenza occurred during this period.

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[3] Boston Med. and Surg. Jour., April, 1905.

Chronic influenza as a contributing or as the sole cause of nervous disease is a subject which has been of interest to me. The merits of the assumption I shall be compelled to depend upon superior authority to prove or disprove. It is without question that organic and inorganic nerve disease results from acute influenza. Whether influenza is the original cause of psychoses acting as a chronic infection, or whether it is the contributing cause to a psychopathic basis, is a question which is beyond my knowledge of psychiatry. The history of influenzal epidemics has shown statistically that the mental and nerve force is lowered for a considerable time after the disappearance of the disease epidemically. A brief resume of a few of the symptoms and sequels, show a predominance of nervous involvement.

Prostration is frequent and far outlasts the symptoms of the disease. Vertigo, insomnia, delirium, and coma are not uncommon. Neuralgic pain is one of the most common disturbances, accompanying, persisting, and recurring irregularly, after the decline of fever and the subsidence of other symptoms. Myalgia, joint pains, hyperesthesia, anesthesia, neuritis may accompany and not infrequently follow attacks for lesser or greater periods. Neurasthenia, or more frequently cerebrasthenia, may be initiated, and the opinion is held that these neuroses are the result of chronic infections by influenza acting directly or through the medium of symptoms of localized inflammation. Epilepsy has immediately followed influenza. To conclude, I have submitted evidence which is far from adequate, but a theory that is strongly in favor of influenza as a chronic as well as an acute disease.

I am of the opinion that influenza is not only with us always as a chronic infection, but it is the source of acute cases occurring sporadically and endemically.

While I have not touched on the invasion of the accessory sinuses by the organism, in closing some consideration should be given this most frequent complication, or rather extension, of the local inflammation. Bacillus influenzæ is responsible for a very large majority of cases of sinusitis, otitis, salpingitis, mastoiditis, and their sequels. The organism has been recovered in the discharge of more than 50 per cent. of patients suffering from suppurative otitis media, usually mixed with the pyogenic organisms. Dench claims that most all cases of maxillary sinusitis are the result of influenzal infection, and emphasizes the fact that the organism finally produces a low grade of inflammation with the formation of polyps and hypertrophy.

REVIEWS.

A SYSTEM OF MEDICINE. By Many Writers. Edited by SIR CLIFFORD ALLBUTT, K.C.B., Regius Professor of Physic in the University of Cambridge; and HUMPHRY DAVY ROLLESTON, M.D., Senior Physician to St. George's Hospital, London. Vol. VI; pp. 861. London: Macmillan & Co., 1909.

VOLUME VI of Allbutt and Rolleston's *System of Medicine* is devoted to diseases of the heart and bloodvessels—a convenient and appropriate arrangement. The volume opens with a brief though interesting chapter on the physics of the circulation, by James Mackenzie; this comprises a revision and amplification of Professor Sherrington's original introductory chapter on cardiac physics—added to, however, by some discussion of the peripheral circulation and blood pressure. Diseases of the pericardium are described very satisfactorily by Frederick T. Roberts, and the clinical descriptions are enhanced by several effective illustrations. Sir R. Douglas Powell discusses diseases of the myocardium and angina pectoris. It is, of course, difficult to separate diseases of the myocardium from other disorders of the heart, and the effort to do this is perhaps responsible for what seems to be a fragmentary and somewhat disconnected discussion. Amends, however, are made in the article on angina pectoris; although, here also one can scarcely escape the conviction that a little too much is made of angina pectoris vasomotoria. What is described as angina pectoris gravior is divided into secondary cardiac angina and primary cardiac angina—both well and ably discussed—albeit one may not be able always to make a differential diagnosis during life. Attention is directed to the fact that all too generally the outlook is deemed exceedingly grave, whereas, by resort to appropriate treatment, much may be done, not only to relieve symptoms, but to remedy the conditions which underlie them.

The volume owes much of its value to the two regius professors of physic who adorn the English profession. Professor Allbutt himself contributes articles on overstress of the heart, disease of the aortic area, and functional disorders. As is well known, he has devoted much time and patient thought to the study and investigation of the effect of mechanical strain on the heart and bloodvessels, and he has repeatedly given to the profession the results of his time and